

#5

|   |                                 |                          |
|---|---------------------------------|--------------------------|
| Form PTO 1449 US Department of<br>Commerce Patent<br>and Trademark<br>Office<br>DEC 26 2001<br>INFORMATION DISCLOSURE<br>STATEMENT BY APPLICANT | ATTY DOCKET NO:<br>P-AR 4802    | SERIAL NO:<br>09/942,098 |
|   | APPLICANT:<br>Steward et al.    |                          |
|   | FILING DATE:<br>August 28, 2001 | GROUP:<br>1645           |

RECEIVED  
DEC 27 2001  
TECH CENTER 1600/2900

### U.S. PATENT DOCUMENTS

| EXAM.<br>INITIALS | DOCUMENT<br>NUMBER | DATE       | NAME                      | CLASS | SUB-<br>CLASS | FILING<br>DATE |
|-------------------|--------------------|------------|---------------------------|-------|---------------|----------------|
| <i>mm</i>         | 5,965,699          | 10/12/1999 | Schmidt<br>and<br>Bostian | 530   | 326           | 11/06/1996     |
| <i>mm</i>         | 5,989,545          | 11/23/1999 | Foster et<br>al.          | 424   | 183.1         | 04/16/1996     |
| <i>mm</i>         | 5,962,637          | 10/05/1999 | Shone et<br>al.           | 530   | 329           | 12/03/1996     |
| <i>mm</i>         | 5,981,200          | 11/09/1999 | Tsien et<br>al.           | 435   | 7.4           | 01/31/1997     |
| <i>mm</i>         | 6,043,042          | 03/28/2000 | Shone et<br>al.           | 435   | 7.1           | 01/30/1998     |

### FOREIGN PATENT DOCUMENTS

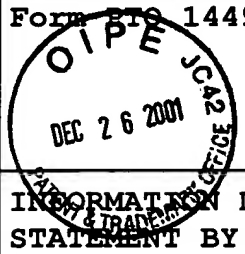
| EXAM.<br>INITIALS | DOCUMENT<br>NUMBER | DATE       | COUNTRY | CLASS | SUB-<br>CLASS | TRANS-<br>LATION<br>YES/NO |
|-------------------|--------------------|------------|---------|-------|---------------|----------------------------|
| <i>mm</i>         | WO 95/33850        | 12/14/1995 | PCT     |       |               |                            |










### OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages)

|           |  |
|-----------|--|
| <i>mm</i> | Anne et al., "High-Throughput Fluorogenic Assay for Determination of Botulinum Type B Neurotoxin Protease Activity," <u>Analytical Biochemistry</u> 291:253-261 (2001) |
| <i>mm</i> | Clegg, "Fluorescence Resonance Energy Transfer," <u>Current Opinion in Biotechnology</u> 6:103-110 (1995)  |

|                                   |                                |
|-----------------------------------|--------------------------------|
| EXAMINER <i>N. M. Springfield</i> | DATE CONSIDERED <i>9/28/03</i> |
|-----------------------------------|--------------------------------|

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

|   |  |                                 |  |
|---|--|---------------------------------|--|
| Form <del>PTO</del> 1449<br><br>INFORMATION DISCLOSURE<br>STATEMENT BY APPLICANT | US Department of<br>Commerce Patent<br>and Trademark<br>Office | ATTY DOCKET NO:<br>P-AR 4802    | SERIAL NO.<br>09/942 <del>0943</del>           |
|   | APPLICANT:<br>Steward et al.                                   |                                 | DEC 27 2001                                    |
|   |  | FILING DATE:<br>August 28, 2001 | GROUP <del>TECH</del> CENTER 1600/2900<br>1645 |

|   |   |
|---|---|
|    | Cornille et al., "Solid-Phase Synthesis, Conformational Analysis and <i>In Vitro</i> Cleavage of Synthetic Human Synaptobrevin II 1-93 by Tetanus Toxin L Chain," <u>Eur. J. Biochem.</u> 222:173-181 (1994)                    |
|    | Ekong et al., "Recombinant SNAP-25 is an Effective Substrate for <i>Clostridium botulinum</i> Type A Toxin Endopeptidase Activity <i>in vitro</i> ," <u>Microbiology</u> 143:3337-3347 (1997)                                   |
|    | Florentin et al., "A Highly Sensitive Fluorometric Assay for 'Enkephalinase,' a Neutral Metalloendopeptidase That Releases Tyrosine-Glycine-Glycine from Enkephalins," <u>Analytical Biochemistry</u> 141:62-69 (1984)          |
|   | Foran et al., "Differences in the Protease Activities of Tetanus and Botulinum B Toxins Revealed by the Cleavage of Vesicle-Associated Membrane Protein and Various Sized Fragments," <u>Biochemistry</u> 33:15365-15374 (1994) |
|  | Geoghegan et al., "Fluorescence-based Continuous Assay for the Aspartyl Protease of Human Immunodeficiency Virus-1," <u>FEBS</u> 262:119-122 (1990)   |
|  | Goudreau et al., "Dns-Gly-(p-NO <sub>2</sub> )Phe-βAla, a Specific Fluorogenic Substrate for Neutral Endopeptidase 24.11," <u>Analytical Biochemistry</u> 219:87-95 (1994)  |
|  | Hallis et al., "Development of Novel Assays for Botulinum Type A and B Neurotoxins Based on Their Endopeptidase Activities," <u>J. Clin. Microbiol.</u> 34:1934-1938 (1996)   |
|  | Hanson and Stevens, "Cocrystal Structure of Synaptobrevin-II Bound to Botulinum Neurotoxin Type B at 2.0 Å Resolution," <u>Nature Structural Biology</u> 7:687-692 (2000)   |
|  | Hodel, "Molecules in Focus: SNAP-25," <u>J. Biochem. &amp; Cell Biol.</u> 30:1069-1073 (1998)   |

|  |                         |
|--|-------------------------|
| EXAMINER  | DATE CONSIDERED 9/28/03 |
|--|-------------------------|

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

|   |  |                              |                                 |
|---|--|------------------------------|---------------------------------|
| Form PTO 1449<br>DEC 26 2001<br>PATENT AND TRADEMARK OFFICE | US Department of<br>Commerce Patent<br>and Trademark<br>Office | ATTY DOCKET NO:<br>P-AR 4802 | SERIAL NO.<br>09/942,098        |
|   | INFORMATION DISCLOSURE<br>STATEMENT BY APPLICANT               | APPLICANT:<br>Steward et al. | FILING DATE:<br>August 28, 2001 |

|    |  |
|----|--|
| MM | Holskin et al., "A Continuous Fluorescence-Based Assay of Human Cytomegalovirus Protease Using a Peptide Substrate," <u>Analytical Biochemistry</u> 226:148-155 (1995)   |
| MM | Humeau et al., "How Botulinum and Tetanus Neurotoxins Block Neurotransmitter Release," <u>Biochimie</u> 82:427-446 (2000)  |
| MM | Kakiuchi et al., "A High Throughput Assay of the Hepatitis C Virus Nonstructural Protein 3 Serine Proteinase," <u>Journal of Virological Methods</u> 80:77-84 (1999)   |
| MM | Knapp et al., The Crystal Structure of Botulinum Toxin A $\alpha$ zinc Protease Domain, <u>37<sup>th</sup> Annual Meeting of the Interagency Botulism Research Coordinating Committee</u> Asilomar, CA (2000)  |
| MM | Lacy et al., "Crystal Structure of Botulinum Neurotoxin Type A and Implications for Toxicity," <u>Nature Structural Biology</u> 5:898-902 (1998)   |
| MM | Le Bonniec et al., "Characterization of the P <sub>2</sub> ' and P <sub>3</sub> ' Specificities of Thrombin Using Fluorescence-Quenched Substrates and Mapping of the Subsites by Mutagenesis," <u>Biochemistry</u> 35:7114-7122 (1996)                          |
| MM | Matayoshi et al., "Novel Fluorogenic Substrates for Assaying Retroviral Proteases by Resonance Energy Transfer," <u>Science</u> 247:954-958 (1990)   |
| MM | Matsumoto et al., "A High-Throughput Screening Utilizing Intramolecular Fluorescence Resonance Energy Transfer for the Discovery of the Molecules that Bind HIV-1 TAR RNA Specifically," <u>Bioorganic &amp; Medicinal Chemistry Letters</u> 10:1857-1861 (2000) |
| MM | Mahajan et al., "Novel Mutant Green Fluorescent Protein Protease Substrates Reveal the Activation of Specific Caspases During Apoptosis," <u>Chemistry &amp; Biology</u> 6:401-409 (1999)  |

|                              |                                |
|------------------------------|--------------------------------|
| EXAMINER <i>MM Mansfield</i> | DATE CONSIDERED <i>9/28/03</i> |
|------------------------------|--------------------------------|

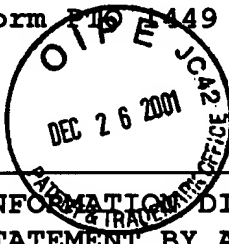
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.





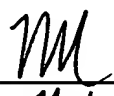

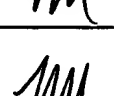
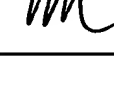
|   |  |                                 |
|---|--|---------------------------------|
| <b>Form PTO 1449</b> <b>US Department of<br/>Commerce Patent<br/>and Trademark<br/>Office</b> | <b>ATTY DOCKET NO:</b><br>P-AR 4802    | <b>SERIAL NO.</b><br>09/942,098 |
|   | <b>APPLICANT:</b><br>Steward et al.    |                                 |
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b>                                      | <b>FILING DATE:</b><br>August 28, 2001 | <b>GROUP:</b><br>1645           |

|          |  |
|----------|--|
| <i>M</i> | Montecucco and Schiavo, "Structure and Function of Tetanus and Botulinum Neurotoxins," <u>Quarterly Reviews of Biophysics</u> 28:423-472 (1995)  |
| <i>M</i> | Niemann et al., "Clostridial Neurotoxins: New Tools for Dissecting Exocytosis," <u>Trends in Cell Biology</u> 4:179-185 (1994)   |
| <i>M</i> | Olsen et al., "High-throughput Screening of Enzyme Libraries," <u>Curr. Opin. Biotechnol.</u> 11:331-337 (2000)  |
| <i>M</i> | Pellizzari et al., "Tetanus and Botulinum Neurotoxins: Mechanism of Action and Therapeutic Uses," <u>Phil. Trans. R. Soc. Lond.</u> 354:259-268 (1999)   |
| <i>M</i> | Rossetto et al., "Tetanus and Botulinum Neurotoxins: Turning Bad Guys Into Good by Research," <u>Toxicon</u> 39:27-41 (2001)   |
| <i>M</i> | Schmidt et al., "Type A Botulinum Neurotoxin Proteolytic Activity: Development of Competitive Inhibitors and Implications for Substrate Specificity at the S <sub>1</sub> ' Binding Subsite," <u>FEBS Lett.</u> 435:61-64 (1998) |
| <i>M</i> | Schmidt and Bostian, "Proteolysis of Synthetic Peptides by Type A Botulinum Neurotoxin," <u>Journal of Protein Chemistry</u> 14:703-708 (1995)   |
| <i>M</i> | Schmidt and Bostian, "Endoproteinase Activity of Type A Botulinum Neurotoxin: Substrate Requirements and Activation by Serum Albumin," <u>Journal of Protein Chemistry</u> 16:19-26 (1997)                                       |
| <i>M</i> | Selvin, "The Renaissance of Fluorescence Resonance Energy Transfer," <u>Nature Structural Biology</u> 7:730-734 (2000)   |
| <i>M</i> | Shone et al., "Proteolytic Cleavage of Synthetic Fragments of Vesicle-Associated Membrane Protein, Isoform-2 by Botulinum Type B Neurotoxin," <u>Eur. J. Biochem.</u> 217:965-971 (1993)   |

|                                     |  |
|-------------------------------------|--|
| <b>EXAMINER</b> <i>NM Hingfield</i> | <b>DATE CONSIDERED</b><br><i>9/28/03</i> |
|-------------------------------------|--|

EXAMINER: Initial of citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

|   |  |                              |                                 |
|---|--|------------------------------|---------------------------------|
| Form <b>P 1449</b><br> | US Department of<br>Commerce Patent<br>and Trademark<br>Office | ATTY DOCKET NO:<br>P-AR 4802 | SERIAL NO.<br>09/942,098        |
| INFORMATION DISCLOSURE<br>STATEMENT BY APPLICANT  |  | APPLICANT:<br>Steward et al. | FILING DATE:<br>August 28, 2001 |
|   |  | GROUP:<br>1645               |                                 |

|   |   |
|---|---|
|    | Sittampalam et al., "High-Throughput Screening: Advances in Assay Technologies," <u>Current Opinion in Chemical Biology</u> 1:384-391 (1997)  |
|    | Swaminathan and Eswaramoorthy, "Structural Analysis of the Catalytic and Binding Sites of <i>Clostridium botulinum</i> Neurotoxin B," <u>Nature Structural Biology</u> 7:693-699 (2000)   |
|    | Tawa et al., "Quantitative Analysis of Fluorescent Caspase Substrate Cleavage in Intact Cells and Identification of Novel Inhibitors of Apoptosis," <u>Cell Death and Differentiation</u> 8:30-37 (2001)                                      |
|   | Vaidyanathan et al., "Proteolysis of SNAP-25 Isoforms by Botulinum Neurotoxin Types A, C and E: Domains and Amino Acid Residues Controlling the Formation of Enzyme-Substrate Complexes and Cleavage," <u>J. Neurochem.</u> 72:327-337 (1999) |
|  | Vitiello et al., "Intracellular Ribozyme-Catalyzed Trans-Cleavage of RNA Monitored by Fluorescence Resonance Energy Transfer," <u>RNA</u> 6:628-637 (2000)  |
|  | Wang et al., "A Continuous Fluorescence Assay of Renin Activity," <u>Analytical Biochemistry</u> 210:351-359 (1993)   |
|  | Wu and Brand, "Resonance Energy Transfer: Methods and Applications," <u>Analytical Biochemistry</u> 218:1-13 (1994)   |
|  | Yamasaki et al., "Cleavage of Members of the Synaptobrevin/VAMP Family by Types D and F Botulinum Neurotoxins and Tetanus Toxin," <u>J. Biol. Chem.</u> 269:12764-12772 (1994)  |

|  |                            |
|--|----------------------------|
| EXAMINER  | DATE CONSIDERED<br>9/28/03 |
|--|----------------------------|

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.